

filed February 27, 1996, now issued as U.S. Patent No. 5,876,453, which, in turn, claims priority to PCT/US95/15576 and is a continuation-in-part of U.S. Application No. 08/351,214, the parent of U.S. Application No. 08/650,594, now issued as U.S. Patent No. 5,603,338.--

At page 3, at the end of line 11, delete "and".

At page 3, lines 23-24, please change "copending U.S. patent application Serial No. 08/607,903" to --U.S. Patent No. 5,876,453--.

At page 3, line 13, after the paragraph ending with "the dental implant of FIG. 1." please insert the following:

--FIGS. 3A and 3B are scanning electron micrographs ("SEMs") of two titanium dental implants prepared in accordance with the present invention;

FIGS. 4A and 4B are SEMs of the same implants shown in FIGS. 3A and 3B, at a higher magnification level;

FIG. 5 is a graph of the results of an Auger electron spectroscopic analysis of a titanium surface that has been exposed to air;

FIGS. 6A and 6B are SEMs of two titanium dental implants prepared in accordance with the present invention; and

FIGS. 7A and 7B are SEMs of the same implants shown in FIGS. 7A and 7B, at a higher magnification level--

At page 4, line 21, after the paragraph ending with "may be left smooth." please insert the following:

--The manner in which the surface of the implant is roughened and the resulting surface topography will now be described. According to one aspect of the present invention, the native oxide layer is removed from the surface of a titanium implant prior to the final treatment of the surface to achieve the desired topography. After the native oxide layer is removed, a further and different treatment of the surface is carried out in the absence of unreacted oxygen to prevent the oxide layer from re-

forming until after the desired surface topography has been achieved. It has been found that this process permits the production of unique surface conditions that are substantially uniform over the implant surface that is so treated.

Removal of the native oxide layer can be effected by immersing the titanium implant in an aqueous solution of hydrofluoric (HF) acid at room temperature to etch the native oxide at a rate of at least about 100 Angstroms per minute. A preferred concentration for the hydrofluoric acid used in this oxide removal step is 15% HF/H₂O. This concentration produces an etch rate of approximately 200-350 Angstroms per minute at room temperature, without agitation, so that a typical native oxide layer having a thickness in the range from about 70 to about 150 Angstroms can be removed in about one-half minute. Other suitable etching solutions for removing the native oxide layer, and their respective etch rates, are:

2
B
50% HF--etch rate about 600 to 750 Angstroms/min.

30% HF--etch rate about 400 to 550 Angstroms/min.

10% HF--etch rate about 100 to 250 Angstroms/min.

A 100% HF was found to be difficult to control, and the etch rate was not determined. The preferred 15% HF solution allows substantially complete removal of the native oxide layer with minimum further consumption of the titanium surface after the implant is removed from the solution.

The native oxide layer may be removed by the use of other acids, or by the use of techniques other than acid etching. For example, the Swart et al. article cited above mentions the use of plasma cleaning to remove thin oxides. Regardless of what technique is used, however, it is important to remove substantially all the native oxide from the implant surface that is intended to interface with the living bone, so that the subsequent treatment of that surface produces a substantially uniform surface texture

to promote uniform bonding to the living bone. The native oxide layer is preferably removed from substantially the entire bone-interfacing surface of the implant. In the case of screw-type dental implants, the bone-interfacing surface typically includes the entire implant surface beyond a narrow collar region on the side wall of the implant at the gingival end thereof. This narrow collar region preferably includes the first turn of the threaded portion of the implant. It is preferred not to etch the gingival end itself, as well as the narrow collar region, because these portions of the implant are normally fabricated with precise dimensions to match abutting components which are eventually attached to the gingival end of the implant. Moreover, it is preferred to have a smooth surface on that portion of a dental implant that is not embedded in the bone, to minimize the risk of infection.

The treatment that follows removal of the native oxide layer must be different from the treatment that is used to remove the native oxide layer. A relatively aggressive treatment is normally required to remove the oxide layer, and such an aggressive treatment does not produce the desired uniform surface texture in the resulting oxide-free surface. Thus, after the native oxide layer has been removed, the resulting implant surface is immediately rinsed and neutralized to prevent any further attack on the implant surface. The surface is then subjected to the further, and different, treatment to produce a desired uniform surface texture. For example, the preferred further treatment described below is a relatively mild acid-etching treatment which forms a multitude of fine cone-like structures having relatively uniform, small dimensions. Because of the prior removal of the native oxide layer, even a mild second treatment of the implant surface can produce a substantially uniform effect over substantially the entire bone-interfacing surface of the implant.

Prior to removing the native oxide layer, the oxide-bearing surface may be grit blasted, preferably with grit made of titanium or a dilute titanium alloy. As is taught in the U.S. Patent No. 5,607,480, the use of a grit made of titanium avoids contaminating the surface of a titanium implant. Thus, for a dental implant made of commercially pure ("CP") titanium, the blasting material may be CP B299 SL grade titanium grit.

The preferred particle size for this grit is in the range from about 10 to about 60 microns (sifted), and the preferred pressure is in the range from about 50 to about 80 psi.

The surface treatment that follows removal of the native oxide layer from the implant surface may take several forms, singly or in combination. The preferred treatment is a second acid etching step, using an etch solution ("Modified Muriaticetch") consisting of a mixture of two parts by volume sulfuric acid (96% by weight H₂ SO₄, 4% by weight water) and one part by volume hydrochloric acid (37% by weight HCl, 63% by weight water) at a temperature substantially above room temperature and substantially below the boiling point of the solution, preferably in the range from about 60°C to about 80°C. This mixture provides a sulfuric acid/hydrochloric acid ratio of about 6:1. This preferred etch solution is controllable, allowing the use of bulk etch times in the range from about 3 to about 10 minutes. This solution also can be prepared without the risk of violent reactions that may result from mixing more concentrated HCl solutions (e.g., 98%) with sulfuric acid. This second etching treatment is preferably carried out in the absence of unreacted oxygen, and before the implant surface has been allowed to re-oxidize, following removal of the native oxide layer. Of course, the implants may be kept in an inert atmosphere or other inert environment between the two etching steps.

The second etching step produces a surface topography that includes many fine projections having a cone-like aspect in the sub-micron size range. Because of the fine roughness of the surface, and the high degree of uniformity of that roughness over the treated surface, the surface topography produced by this process is well suited for osseointegration with adjacent bone. As illustrated by the working examples described below, the final etched surface consists of a substantially uniform array of irregularities having peak-to-valley heights of less than about 10 microns. Substantial numbers of the irregularities are substantially cone-shaped elements having base-to-peak heights in the range from about 0.3 microns to about 1.5 microns. The bases of these cone-shaped elements are substantially round with diameters in the range from

about 0.3 microns to about 1.2 microns, and spaced from each other by about 0.3 microns to about 0.75 microns. The SEMs discussed below, and reproduced in the drawings, illustrate the surface topography in more detail.

The acid-etched surface described above also provides a good site for the application of various materials that can promote bonding of the surface to adjacent bone.

Examples of such materials are bone-growth-enhancing materials such as bone minerals, bone morphogenic proteins, hydroxyapatite, whitlockite, and medicaments. These materials are preferably applied to the etched surface in the form of fine particles which become entrapped on and between the small cone-like structures. The bone-growth-enhancing materials are preferably applied in the absence of oxygen, e.g., using an inert atmosphere.

The roughness of the surface to which these materials are applied enhances the adherence of the applied material to the titanium implant. The uniformity of the rough surface enhances the uniformity of the distribution of the applied material, particularly when the material is applied as small discrete particles or as a very thin film.

A preferred natural bone mineral material for application to the etched surface is the mineral that is commercially available under the registered trademark "BIO-OSS". This material is a natural bone mineral obtained from bovine bone; it is described as chemically comparable to mineralized human bone with a fine, crystalline biological structure, and able to support osseointegration of titanium fixtures.

The invention will be further understood by reference to the following examples, which are intended to be illustrative and not limiting:

EXAMPLE NO. 1

A batch of 30 screw-type cylindrical implants made of CP titanium were grit blasted using particles of CP B299 SL grade titanium grit having particle sizes ranging from

10 to 45 microns, at a pressure of 60 to 80 psi. After grit-blasting, native oxide layer was removed from the implant surfaces by placing 4 implants in 100 ml. of a 15% solution of HF in water at room temperature for 30 seconds. The implants were then removed from the acid, neutralized in a solution of baking soda, and placed in 150 ml. of "Modified Muriaticetch" (described above) at room temperature for 3 minutes. The implants were then removed from the acid, neutralized, rinsed and cleaned. All samples displayed very similar surface topographies and a high level of etch uniformity over the surface, when compared with each other in SEM evaluations. Consistency in the surface features (peaks and valleys) was also observed. The SEMs in FIGS. 3A, 3B, 4A and 4B show the surfaces of two of the implants, Sample A-1 and Sample A-4, at magnifications of 2,000 and 20,000. It will be observed that the surface features over the areas shown are consistent and uniform. The scale shown on the X20,000 photographs is 1 micron=0.564 inch. At this magnification the surfaces appear to be characterized by a two-dimensional array of cones ranging in height (as seen in the SEMs) from about 0.17 inch to about 0.27 inch; the base diameters of these cones varied from about 0.17 inch to about 0.33 inch. Converting these numbers to metric units on the above-mentioned scale (1 micron=0.564 inch) yields:

cone height range (approx.)=0.30 to 0.50 micron

cone base diameter range (approx.)=0.30 to 0.60 micron.

The same degree of uniformity was found in all the samples, and from sample to sample, at magnifications of 2,000 and 20,000, as compared with similar samples subjected to bulk etching without prior removal of the native oxide, as described in EXAMPLE NO. 2 below.

EXAMPLE NO. 2

Four of the implants that had been grit blasted as described in EXAMPLE NO. 1 above were placed in 150 ml. of "Modified Muriaticetch" for 10 minutes. The

implants were then removed, neutralized, rinsed and cleaned. SEM photographs taken at magnifications of 2,000 and 20,000 showed that the bulk etch solution failed to remove the native oxide layer after 10 minutes in the etch solution. The failure to remove the native oxide layer (100-150 Angstrom units thick) resulted in a non-uniformly etched surface, as depicted for example in FIG. 3 of U.S. Patent No. 5,876,453. In areas of the implant surfaces where the native oxide was removed, the topography was similar to that observed on the implants in EXAMPLE NO. 1.

EXAMPLE NO. 3

The procedure of this example is currently preferred for producing commercial implants. A batch of screw-type implants made of CP titanium were immersed in a 15% solution of HF in water at room temperature for 60 seconds to remove the native oxide layer from the implant surfaces. A plastic cap was placed over the top of each implant to protect it from the acid. The implants were then removed from the acid and rinsed in a baking soda solution for 30 seconds with gentle agitation. The implants were then placed in a second solution of baking soda for 30 seconds, again with agitation of the solution; and then the implants were rinsed in deionized water. Next the implants were immersed in another solution of two parts by volume sulfuric acid (96% by weight H₂ SO₄, 4% by weight water), and one part by volume hydrochloric acid (37% by weight HCl, 63% by weight water) at 70°C for 5 minutes. The implants were then removed from the acid and rinsed and neutralized by repeating the same steps carried out upon removal of the implants from the HF. All samples displayed very similar surface topographies and a high level of etch uniformity over the surface, when compared with each other in SEM evaluations. Consistency in the surface features (peaks and valleys) was also observed. The SEMs in FIGS. 6A, 6B, 7A and 7B show the surfaces of two of the implants, Sample 705MB and Sample 705MC, at magnifications of 2,000 and 20,000. It will be observed that the surface features over the areas shown are consistent and uniform. The scale shown on the X20,000 photographs is 1 micron=0.564 inch. At this magnification the surfaces appear to be characterized by a two-dimensional array of cones ranging in height (as seen in the